ANDA 75-040 November 24, 1999

ESI Lederle
Attention: J. Barton Kalis
2 Esterbrook Lane
Cherry Hill, NJ 08003-4099

Dear Sir:

This is in reference to your abbreviated new drug application dated December 26, 1996, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Propofol Injectable Emulsion, 10 mg/mL, packaged in vials.

Reference is also made to your amendments dated January 27, May 14 and October 7, 1998; and July 29, September 16, and November 24, 1999.

We have completed the review of this abbreviated application and have concluded that, based upon the information you have presented to date, the drug is safe and effective for use as recommended in the submitted labeling. Therefore, the application is tentatively approved. This determination is based upon information available to the Agency at this time, (i.e., data in your application and the status of current good manufacturing practices (CGMPs) of the facilities used in the manufacture and testing of the drug product), and is subject to change on the basis of new information that may come to our attention.

The reference listed drug product (RLD) upon which you have based your application, Diprivan Injectable Emulsion of Zeneca Ltd., is currently subject to a period of patent protection (U.S. Patents No. 5,714,520, 5,731,355, 5,731,356, and 5,908,869). As noted in the Agency's publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations", this period was scheduled to expire on March 22, 2015. However, the period has been extended under Section 111 of the Food and Drug Administration Modernization Act (21 U.S.C. 355a (1997) for an additional 6 months. Your application contains a Paragraph III Certification to each of these patents under Section 505(j)(2)(A)(vii)(III) of the Act

stating that you will not market this drug product prior to the expiration of these patents. Therefore, final approval of your application may not be made effective pursuant to 21 U.S.C. 355(j)(5)(B)(ii) of the Act until the period has expired, i.e., September 22, 2015.

To provide for final approval of this application, please submit an amendment at least 60 (but not more than 90) days prior to the date you believe your application will be eligible for final approval. This amendment should identify changes, if any, in the conditions under which the product was tentatively approved, and should include updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. An amendment should be submitted even if none of these changes were made. The amendment should be designated clearly in your cover letter as a MINOR AMENDMENT. In addition to this amendment, the Agency may request that you submit an amendment containing the same information at any time prior to the final approval date.

Failure to submit such amendments requested by the agency will prompt a review of the application which may result in rescission of the tentative approval status of your application, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this abbreviated application as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (CGMPs) are subject to Agency review before final approval of the application will be made.

Please note that this drug product may not be marketed without final Agency approval under Section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under Section 501 of the Act and 21 U.S.C. 331(d). Also, until the Agency issues the final approval letter, this drug product will not be deemed approved for marketing under
21 U.S.C. 355 and will not be listed in the "Approved Drug Products with Therapeutic Equivalence Evaluations" list (the "Orange Book"), published by the Agency. Should you believe that there are grounds for issuing the final approval letter

prior to September 22, 2015, you should amend your application accordingly.

At the time you submit any amendments, please contact Kassandra Sherrod, Project Manager, at (301) 827-5849, for further instructions.

Sincerely yours,

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research